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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,518	08/24/2001	Mark J. Jaroszeski	1372.34	2429
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SMITH HOPEN, PA 180 PINE AVENUE NORTH OLDSMAR, FL 34677				
EXAMINER				
ANGELL, JON E				
ART UNIT		PAPER NUMBER		
1635				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/939,518

Applicant(s)

JAROSZESKI ET AL.

Examiner

J. E. Angell

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 6, 8, 10, 21, 22 and 24-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6, 8, 10, 21, 22 and 24-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Claims 1, 2, 6, 8, 10, 21, 22, 24-28 are currently pending and are addressed herein.

Applicants appealed the rejection of the instant claims under 35 U.S.C. 102(e) as being anticipated by Dimmer (U.S. Patent 6,678,558 B1) to The Board of Patent Appeals and Interferences (hereafter "The Board"). The Board rendered a decision on September 2, 2008, reversing the rejection. The Board did not submit comment on the instant claims being obvious over the teaching of Dimmer when used in combination with another reference, such as Hofmann (see below). In light of The Board's decision, and upon further consideration of the claims and Dimmer, the instant Action is deemed appropriate and does not conflict with the Board's decision.

This Office Action supersedes the previous Action, and the time period for response is re-set to begin again with the mailing of this Action.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 2, 6, 8, 10, 21, 22, 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hofmann et al. (U.S. Patent 6,055,453, previously of record) in view of Dimmer et al. (U.S. Patent 6,678,558 B1, previously of record).

Hofmann teaches a method for facilitating a delivery of a desired molecule such as nucleic acids, antisense nucleic acids, Ribozymes, polypeptides, and polynucleotides into a target tissue comprising a cell (see col. 12, lines 14 and 34; col. 13, lines 13, 24 and 31-31); and applying a single continuous electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example, see column 10, lines 3-56; and col. 11, lines 63-65). Hofmann explicitly teaches that there can be any "number of desired pulses, typically one to 100 pulses per second." (See column 10, lines 12-13). Hofmann explicitly teaches that the electric field can have a field strength comprising 10V/cm-20kV/cm and can be applied for 10 μ s-100ms (see col. 10, lines 3-41). Hofmann teaches that the electric field can be, for example, a square pulse waveform (see col.10, line 55-56). Hofmann teaches that the introducing step can be by needle injection (i.e. syringe) (see col. 13, lines 31-45). Hofmann also teaches that the target tissue can be skin, tumor, muscle, ovary, prostate, lung, heart, kidney, colon, testis, melanoma, etc. (see col. 14, lines 10-30). Hofmann also specifically teaches, "In a particular

embodiment, it is preferred that when the electric field is low, the pulse length is long." (See column 10, lines 37-39).

Hofmann does not teach applying the pulse for longer than 100ms.

Similarly, Dimmer teaches a method for delivering an agent such as a nucleic acid into a cell of a target tissue (such as skin or tumor tissue) using an electric signal (e.g., see abstract), wherein the agent is injected directly by needle and syringe (e.g., see column 2 lines 24-27), wherein the electric signal can have a bipolar, square or sinusoidal waveform (e.g., see column 5, lines 35-36; column 8, lines 17-30), wherein the electric field(s) are in the range of 1mV/cm to 200V/cm (e.g., 25V/cm or 100V/cm see column 10, lines 29-42). Importantly, Dimmer teaches:

The efficiency of cell electroporation increases as the energy field between the electrodes 16 increases. The energy field created between two electrodes 16 can be determined according to Equation 2, where E is the electric field, V is the potential between the two electrodes 16, r is the diameter of an electrode and D is the displacement between the electrode centers.

$E = V / (2r \ln(D/r))$ (2) (See column 10, lines 20-27);

As the electric field increases, the total electroporation signal duration can be decreased in order to prevent excessive amounts of energy from being delivered to the treatment site 30. The total electroporation signal duration is preferably less than about 10 seconds, more preferably about 30 μ s-10 seconds, even more preferably about 30 μ s-1ms and most preferably about 50 μ s-400ms. (See column 20, lines 38-44);

Claim 5 of Dimmer reads: "A method according to claim 1 wherein the therapeutic electric signal is comprised of 1 to about 1,000,000 pulses."

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of Hofmann and Dimmer to create the claimed invention wherein application of a single continuous electric field in the range of 1V/cm to 200 V/cm is applied for a duration in the range of 200ms to 20 minutes can effect a change in

the porosity of a cell sufficient to facilitate entry of a desired molecule into an interior of the cell, with a reasonable expectation of success.

Hofmann provides an explicit teaching that when low electric fields are used, longer pulses should be used. Specifically Hofmann teaches, "[I]t is preferred that when the electric field is low, the pulse length is long." (See column 10, lines 37-39). Therefore, Hofmann provides a motivation to use low electric fields for longer durations of time. Furthermore, since Hofmann teaches that applying an electric field within the claimed range for a duration of 100ms is sufficient to change the porosity of a cell membrane to allow entry of a molecule into a cell, it would be expected that increasing the length of the pulse to more than 200ms and up to 10 seconds would also be sufficient to facilitate entry of a molecule into a cell.

Therefore, the instant claims are considered to be obvious in view of the teachings of Hofmann and Dimmer.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635

/George C. Elliott, Ph.D./
Director, Technology Center 1600